Complete Summary

GUIDELINE TITLE

Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: recommendations of the HIV Medicine Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group.

BIBLIOGRAPHIC SOURCE(S)

Dube MP, Stein JH, Aberg JA, Fichtenbaum CJ, Gerber JG, Tashima KT, Henry WK, Currier JS, Sprecher D, Glesby MJ. Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: recommendations of the HIV Medicine Association of the Infectious Disease Society of America. Clin Infect Dis 2003 Sep 1;37(5):613-27. [147 references] PubMed

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Dyslipidemia
- Human immunodeficiency virus

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Infectious Diseases
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide a comprehensive approach for evaluation and treatment of dyslipidemia in adults infected with human immunodeficiency virus who are receiving antiretroviral therapy

TARGET POPULATION

Adults with human immunodeficiency virus who are receiving antiretroviral therapy

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Monitoring serum lipid levels and screening of total cholesterol, high-density lipoprotein-cholesterol (HDL-C), triglyceride levels, low-density lipoprotein cholesterol (LDL-C), and non–HDL-C
2. Assess risk factors:
    - Cigarette smoking
    - Hypertension (e.g., blood pressure of 140 mm Hg or receipt of antihypertensive medication)
    - Low high-density lipoprotein cholesterol level (<40 mg/dL)
    - Family history of premature coronary heart disease (CHD) (Male first-degree relative <55 years old or female first-degree relative <65 years old)
    - Age (>45 years for men and >55 years for women)
3. Evaluation of patients for switching antiviral therapies

Treatment/Management

1. Nondrug therapies, attention to modifiable risk factors
    - Smoking cessation
    - Dietary and exercise interventions
        - Fish oils (omega-3 fatty acid supplements)
    - Hormone replacement with estrogen/progestin is not recommended.
2. Drug therapies including:
    - Statins (pravastatin, fluvastatin, simvastatin, lovastatin, atorvastatin)
    - Fibrates (gemfibrozil, micronized fenofibrate)
    - Niacin

- Delavirdine
- Protease inhibitors (nevirapine, abacavir)

3. Monitor drug interactions

MAJOR OUTCOMES CONSIDERED

Rates of cardiovascular morbidity in human immunodeficiency virus (HIV)-infected individuals

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

I. Evidence from ≥1 properly randomized, controlled trial
II. Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
III. Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A working group of clinical scientists, consisting of members of the Cardiovascular Subcommittee of the AIDS Clinical Trials Group, updated the preliminary recommendations to assist clinicians in the evaluation and treatment of lipid disorders among human immunodeficiency virus (HIV)-infected adults. Data regarding the prevalence and incidence of dyslipidemia and cardiovascular disease in HIV-infected patients, pharmacokinetic profiles for hypolipidemic agents, and treatment trials of dyslipidemia in HIV-infected patients were considered.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the quality of the evidence (I-III) and strength of recommendation (A-E) are given at the end of the Major Recommendations.

Effects of Switching Antiviral Therapies

In patients with a favorable treatment history (i.e., no previous receipt of a nucleoside reverse-transcriptase inhibitors (NRTI)-based regimen that was less than fully suppressive and no history of virologic rebound occurring while

receiving treatment), switching from a potentially lipid level-increasing protease inhibitors (PI) to nevirapine or abacavir may be preferable to a pharmacologic intervention with a lipid-lowering drug (C-III).

Evaluation of Patients

Measurement of Lipid Values

- Evaluation of serum lipid levels should be performed after fasting for a minimum of 8 h, and preferably for 12 h, and the levels should be determined before initiation of antiretroviral therapy (B-III).
- The standard screening lipid profile should include measurement of total cholesterol, high-density lipoprotein-cholesterol (HDL-C), and triglyceride levels. Using these measured values, low-density lipoprotein-cholesterol (LDL-C) and non–HDL-C levels are calculated. This should be repeated within 3 to 6 months after the initiation of highly active antiretroviral therapy (HAART), then yearly, unless abnormalities are detected or therapeutic interventions are initiated (B-III).

Treatment

Hypercholesterolemia

- Nondrug therapies
    - Hormone replacement with estrogen/progestin is no longer recommended for primary or secondary coronary heart disease (CHD) prevention (A-I).
- Drug therapies for human immunodeficiency virus (HIV)-infected individuals
    - A statin is a recommended first choice for elevated LDL-C levels or for elevated non–HDL-C levels when triglyceride levels are 200 to 500 mg/dL (B–I).
    - Fibrates are less optimal alternative agents for hypercholesterolemia (C-I).
    - Because niacin causes insulin resistance (even in nondiabetic individuals), it has been suggested that niacin should generally be avoided as first-line therapy for patients receiving PIs or who have lipodystrophy until additional safety data are available (C-III).
    - Use of bile-sequestering resins (cholestyramine, colestipol, and colesevalam) is not recommended (C-III).

Hypertriglyceridemia

- Nondrug therapies
    - Fish oils (omega-3 fatty acid supplements) variably decrease triglyceride synthesis and may be tried (C-III).
- Drug therapies
    - Niacin is effective therapy for hypertriglyceridemia but should be avoided as first-line therapy in patients receiving HIV PIs or who have lipoatrophy (C-III).
    - Statins are not generally recommended as first-line therapy for isolated hypertriglyceridemia, particularly when triglyceride levels are >500 mg/dL (C-III).

Choice of Initial Drug Treatment for Hyperlipidemia

- Elevated LDL-C level or elevated non–HDL-C level with triglyceride level of 200 to 500 mg/dL
    - Either pravastatin, (20–40 mg daily [q.d.] starting dose) (A-I), or atorvastatin (10 mg q.d. starting dose) (B-II) is recommended (see the section Drug-Drug Interaction Considerations, in the original guideline document), along with careful monitoring of virologic status and for hepatic and skeletal muscle toxicity. Fluvastatin (20–40 mg q.d. starting dose) is a reasonable alternative (B-II).
    - A fibrate, either gemfibrozil (600 mg twice a day [b.i.d.]) (B-I) or micronized fenofibrate (54–160 mg q.d.) (B-I), are reasonable alternative agents only when statins are not appropriate.
- Triglyceride level, >500 mg/dL
    - First-line treatment is gemfibrozil (600 mg b.i.d.) given 30 min before morning and evening meals (B-I) or micronized fenofibrate (54–160 mg q.d.) (B-I). Fish oils and niacin are alternative agents (C-III).

Approach to Refractory Disorders

- When used in combination with fibrates, pravastatin (B-I) and fluvastatin (C-III) may be the preferred statins.
- For elevated triglyceride levels that are inadequately responsive to fibrate therapy and maximal lifestyle changes, the addition of a fish oil supplement or niacin can be considered (C-III)

Drug-drug Interaction Considerations

- Simvastatin and lovastatin should not be used in patients taking PIs or delavirdine (E-III) (see table 6 in the original guideline).
- Atorvastatin can probably be used with caution, at low initial doses, in patients taking PIs (B-I), although extensive safety data are lacking.
- Pravastatin appears to be safe for use with PIs (A-I).
- Fluvastatin may also be a safe alternative for use with PIs (B-II) on the basis of its known metabolism and the relative lack of significant interaction with other CYP3A4 and CYP2C9 inhibitors.
- Any of the statins can probably be used safely in persons taking efavirenz or nevirapine (C-III), although more data are needed.

Quality of Evidence

I. Evidence from $\geq$1 properly randomized, controlled trial
II. Evidence from $\geq$1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
III. Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Strength of Recommendation

A. Good evidence to support a recommendation for use

B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for "General Approach to Lipid Disorders and Cardiovascular Risk in HIV-infected Patients Receiving HAART".

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

The close relationship between human immunodeficiency virus (HIV) care providers and their patients affords a major opportunity for primary and secondary prevention of non–HIV-related conditions, such as cardiovascular disease. These recommendations will assist the HIV clinician´s efforts to broaden the health benefits associated with ongoing clinical care for adults in the HIV clinic.

Specific Benefits

- The switching of antiviral therapies has the potential advantage of avoiding pharmacologic intervention for elevations in lipid levels.
- Switching from a protease inhibitor (PI) to nevirapine or abacavir has generally resulted in an improvement in total cholesterol and triglyceride levels.
- Considerable evidence demonstrates the benefits of HMG-CoA reductase inhibitors in both reducing the risk of coronary heart disease (CHD) in patients without prior CHD (primary prevention) and reducing the progression of coronary artery stenoses and risk of recurrent CHD events (secondary prevention).

Subgroups Most Likely to Benefit

Cardiovascular disease occurs earlier and at a higher rate in certain populations, such as black persons, that increasingly overlap with the epidemiology of HIV infection. It is reasonable to anticipate that this problem will worsen in the midst

of the epidemic of obesity and diabetes in the United States and elsewhere, an epidemic that disproportionately affects Hispanic and non-Hispanic black persons.

POTENTIAL HARMS

- Patients who have moderate to severe lipoatrophy should be encouraged to increase physical activity, but excessive weight loss has the potential to exacerbate lipoatrophy.
- Niacin produces frequent cutaneous flushing. Although uncommon, hepatotoxicity can be severe.
- Niacin causes insulin resistance.
- Bile-sequestering resins can be associated with increased triglyceride levels.
- Combination fibrate-statin therapy should be used with great caution because of the risk of myopathy

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Enthusiasm for drug therapy for dyslipidemia should be tempered with the understanding that interventions for advanced immunosuppression, opportunistic infections, malignancies, and human immunodeficiency virus (HIV)-associated wasting should take precedence during the initial stages of treatment. There is currently no evidence that HIV- infected patients should be offered interventions for lipid abnormalities that are more aggressive than those used for the general population.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Dube MP, Stein JH, Aberg JA, Fichtenbaum CJ, Gerber JG, Tashima KT, Henry WK, Currier JS, Sprecher D, Glesby MJ. Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: recommendations of the HIV Medicine Association of the Infectious Disease Society of America. Clin Infect Dis 2003 Sep 1;37(5):613-27. [147 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Sep 1

GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

Cardiovascular Subcommittee of the Acquired Immune Deficiency Syndrome (AIDS) Clinical Trials Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Michael P. Dube, Indiana University, Indianapolis; James H. Stein, University of Wisconsin, Madison; Judith A. Aberg, Washington University, St. Louis, MO; Carl J. Fichtenbaum, University of Cincinnati, OH; John G. Gerber, University of Colorado, Denver; Karen T. Tashima, Brown University, Providence, RI; W. Keith Henry, University of Minnesota, St. Paul; Judith S. Currier, University of California at Los Angeles; Dennis Sprecher, Cleveland Clinic, OH; Marshall J. Glesby, Cornell University, New York

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Infectious Disease Society of America (IDSA) Web site:

- HTML Format
- Portable Document Format (PDF)
- Postscript

Print copies: Available from Infectious Diseases Society of America, 66 Canal Center Plaza, Suite 600, Alexandria, VA 22314.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001 Mar 15;32(6):851-4.

Electronic copies: Available from the Infectious Diseases Society of America (IDSA) Web site:

- HTML Format
- Portable Document Format (PDF)

Print copies: Available from Infectious Diseases Society of America, 66 Canal Center Plaza, Suite 600, Alexandria, VA 22314.

PATIENT RESOURCES

None available

NGC STATUS

This NGS summary was completed by ECRI on May 6, 2004.

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